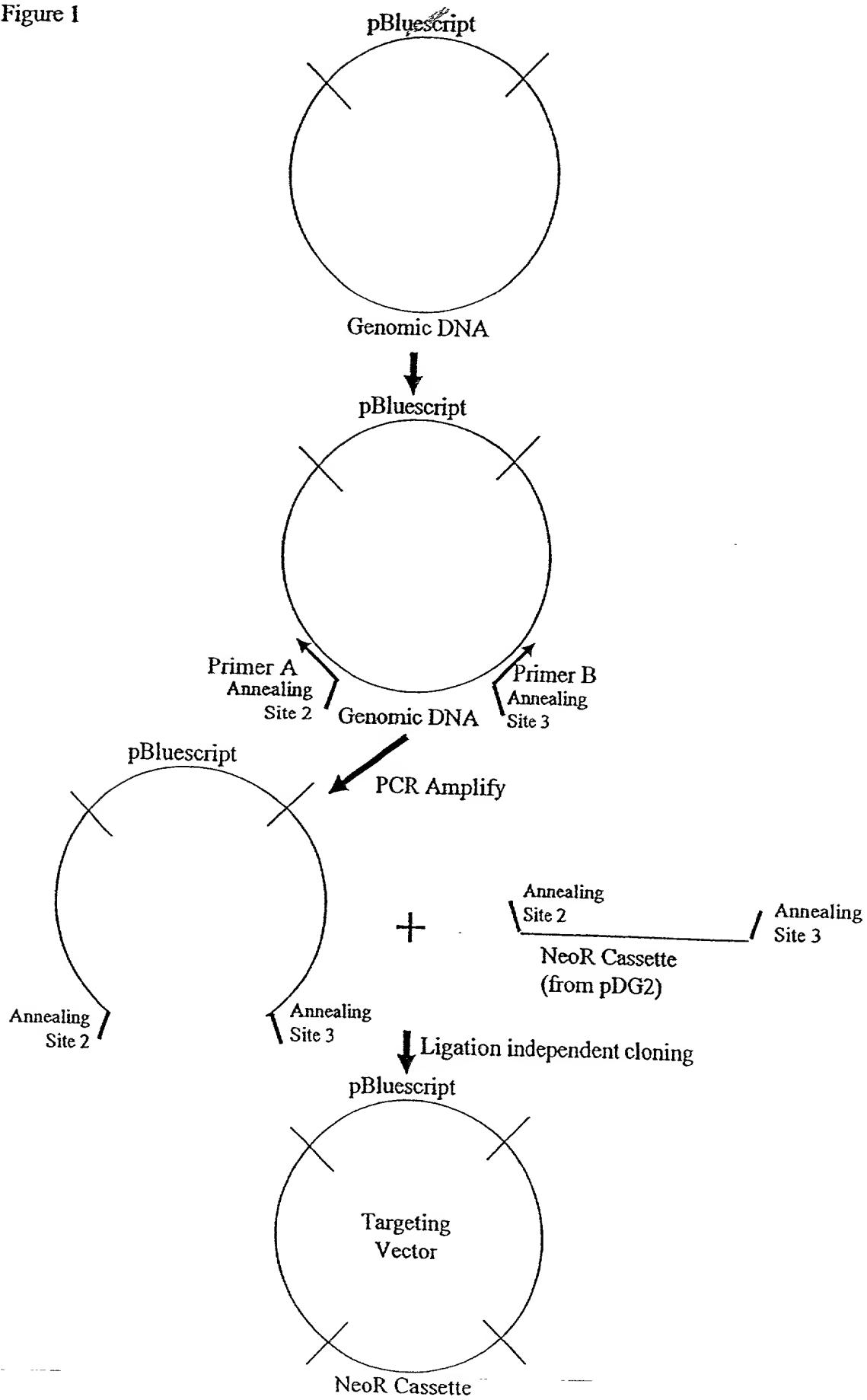


Figure 1



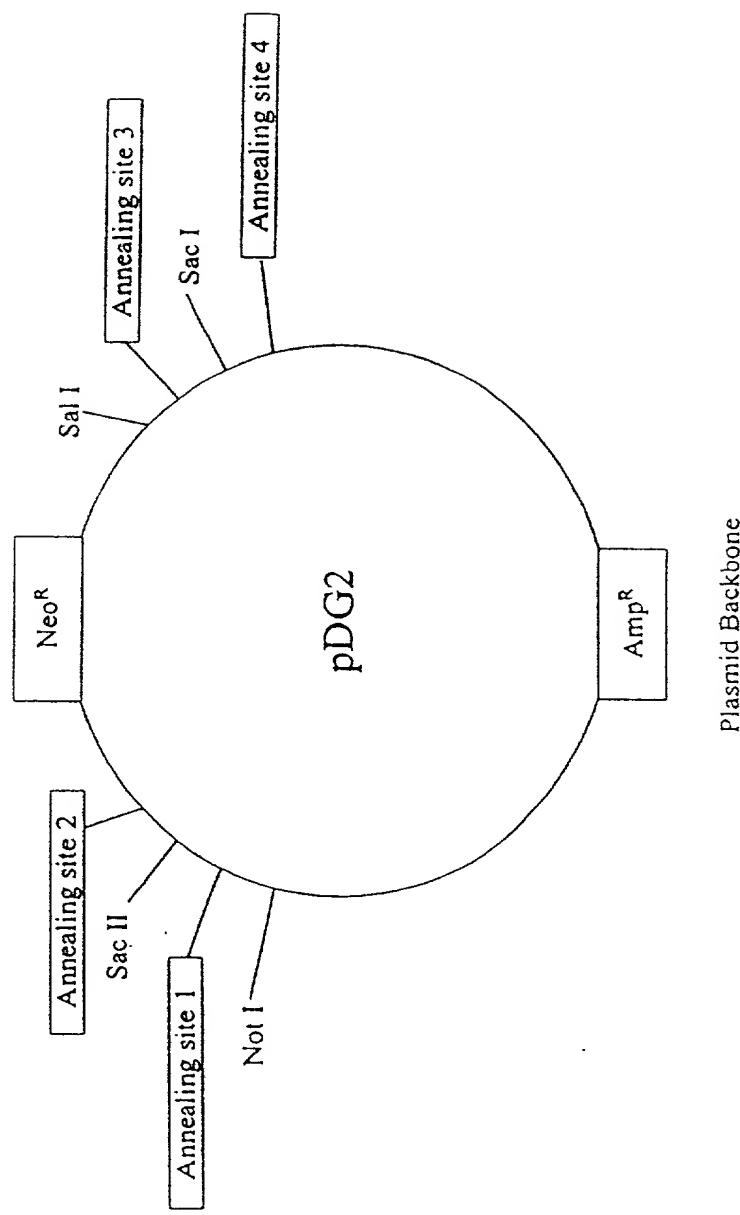


FIGURE 2A

Plasmid Backbone

FIGURE 2B

pDG2.

GTAACTACGTCAGGTGGCACTTTGGGAAATGTGCGCGAACCCCTATTGTTTATTTCTAAATACATTCAAAATA
TGTATCCGCTCATGAGACAATAACCCCTGATAAATGCTTCATAAATATTGAAAAGGAAGAGTATGAGTATTCAACATTTC
CGTGTGCCCTTATTCCCTTTGCGGCATTGCTTCCTGTTTGTCAACCCAGAACGCTGGTAAAGTAAAGA
TGCTGAAGATCAGTTGGGTGACAGTGGTTACATGAACTGGATCTAACAGCGTAAGATCTTGAGAGTTTCGCC
CCGAAGAACGTTCTCCAATGATGAGCACTTTAAAGTTCTGCTATGTGGCGCGTATTATCCGTTGACGCCGGCAA
GAGCAACTCGGTGCCGCATAACTATTCTCAGAATGACTGGTTGAGTACTCACCAAGTCACAGAAAAGCATCTTACGGA
TGGCATGACAGTAAGAGAATTATGCACTGCTGCCATAACCATGAGTATAACACTGCGGCCACTTACTCTGACAACGA
TCGGAGGACGAAGGAGCTAACCGTTTTTGACAAACATGGGGATCATGTAACCTGCCCTGATCGTTGGGAACCGAG
CTGAATGAAGCCATACCAAAACGACGAGCGTACACCAACGATGCTGAGCAATGGCAACAAACGTTGCCAAACTATTAAAC
TGGCGAACTACTTACTCTAGCTCCGGCAACAATTAAAGACTGGATGGGGCGATAAGTTGCAAGGACCACTCTGC
GCTCGGCCCTTCCGGCTGGCTGGTTTATTGCTGATAAATCTGGAGGCCGGTCAAGCTGGTATCATTGAGCA
CTGGGGCCAGTGTAAAGCCCTCCGTTACAGTGTATTCTACACGACGGGAGTCAGGCAACTATGGATGAACGAAATAG
ACAGATCGTCAAGTGGTCACTGATTAAGCATTGTAACGACCAAGTGTACTCATATAACTTTAGATTG
ATTACCCCGTTGATAATCAGAAAAGCCCCAAAAGGAGAAGTGTATAAGCAATTATTAAATTGTAACCGTTAATA
TTTGTAAATTGCGTTAAATTGTTGTTAATCAGCTATTAACTGAAATGCGGAAATCGGAAAATCCCTTAT
AAATCAAAGAAATGCCGAGATAGGGTTGAGTGTGTTCAAGTTGGAACAAAGGTCACATTAAAGAACGTGGACTC
CAACGTCAAAGGCAGAAAACCGTCTATCGGGCGATGGCCACTACGTGAACCATCACCAAAATCAAGTTTGGGT
CGAGGTGCCGTAAGCACTAAATCGGAACCTTAAAGGGAGCCCCGATTAGAGCTGACGGGAAACGCAACGTGGCA
GAAAGGAAGGGAAAGAGCGAAAGGAGCGGGCGTAGGGCGCTGGCAAGTGTAGCGGTACGCTGCCGTAACCACCA
CCCGCCGCGCTTAATCGGCCGCTACAGGGCCGTTAAAGGATCTAGGTAAGATCCTTTGATAATCTCATGACCAAA
TCCCTTAACGTGAGTTTGTGTTCACTGAGCTCAGACCCCTAGAAAAGATCAAAGGATCTCTGAGATCCTTTTT
CTGCGCTAATCTGCTGTTGAAACAAAAAACCCACCGCTACCAGCGTGGTTGTTGCGGATCAAGAGCTACCAAC
TCTTTTCCGAAGGTAACTGGTTCAAGCAGAGCGCAGATAACAAATCTGTTCTAGTGTAGCCGTAGTTAGGCCACC
ACTTCAAGAACTCTGTAAGCCGCTACATCCTGCTCTGTAATCTGTTACCACTGGCTGCTGGCAGTGGCATAAG
TCGTTGCTTACCGGGTTGGACTCAAGACGATAGTTACCGGATAAGGCGCAGCGTGGCTGCTGACACGGGGGTTCTGAC
ACAGCCCAGCTGGAGCGAACGACCTACACCGAACTGAGATACCTACAGCGTGGCTGAGCTATGAGAAAGGCCACGCTCCCG
AAGGGAGAAAGGGACAGGTACCGGTAACCGGAGGGCTGGAAACAGGAGAGCGCACAGGGAGCTCCAGGGGAAAC
GCCTGGTATCTTATAGTCTGCGGTTTCCGACCTCTGACTTGAGCTCGATTTTGATGCTGTCAGGGGCG
GAGCCTATGAAAACGCCAGAACCGGGCTTACCGGTTACACTTATGCTCCGCTCGTATGTTGAGGAGCTTGTG
AGTTAGCTCACTCATTAGGACCCCCAGGTTACACTTATGCTCCGCTCGTATGTTGAGGAGCTTGTG
ACAATTTCACACGAAACGCTATGACCATGATTACGCCAGCTACGTAAACGACTCACTAGGCCCGCGTTAAC
AATGTGCTCCTTTGGCTTGTCTCCGGGCAAGCCAGACAAGAACAGTTGACGTCAGCTTCCCGGACGCGTCT
AGCGCGCGCCGAACTCTGCGAGGATTGAGGGCCCTGAGGTCAATTCTACCGGGTAGGGAGGCGCTTCCAGG
CAGTCTGGAGCATGCGCTTACAGGCCCGCTGGACTTGGCGTACACAAGTGGCTCTGGCGTCCACACATTCCACA
TCCACCGTAGGCCAACCGCTCCGTTTGGCTGGCCCTTCCGCGCACCTCTACTCCTCCCTAGTCAGGAAGTTC
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GGCTGGAAAGGGTGGTCCGGGGGGCTCAGGGCGGGCTCAGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG
GGCATTCTCGCACGCTTCAAAAGCGCACGCTGCTGCTGTTCTCTCATCTCCGGCTTTCGACCTGAGCTCAGC
CAATATGGGATCGGCCATTGAAAGATGGACAGCAGGTTCTCCGGCCCTTGGGTGGAGAGGCTATTGGGCTATG
ACTGGGCAACACAGAAATCGCTGCTGTGATGCCCGTGTCTGGCTGTGAGCGCAGGGGCCGGTTCTTGT
AAGACCGACCTGTCCGGTGCCTGAACTGAGGACGAGGAGCGCGGGCTATGTGGCTGGCCACGACGGCGTTCC
TTGCCAGCTGCTCGACGTTGACTGAAGCGGAAGGGACTGGCTGCTATTGGGCAACTGCCGGGAGGATCTCC
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ACCTGCCATTGACCAACGAAACATGCCATCGAGCGAGCACGTAACCGGATGGAAGCGGCTTGTGATCAGGA
TGATCTGGACGAAAGGACATCAGGGCTCGGCCAGCGAACACTGTTGCCAGGCTCAAGGCGCGATGCCGACGGGATG
ATCTCGCTGACCCATGGCGATGCCGTTGCGAAATATCATGGGAAAATGCCGCTTTCTGATTGATCATGACTGT
GGCCGGCTGGGTGGCGACCGCTACAGGACATAGCGTTGGCTACCGCTGATATTGCTGAAAGAGCTTGGCGGAATG
GGCTGAGGGCTTCTGCTTACGGTATGCCGCTCCGATTCCGAGCGCATGCCCTCTGACCGAGT
TCTTCTGAGGGGATCGATCCGCTGTAAGTCTGAGAAATTGATGCTATTAAACAATAAGATGTCACAAATGG
AAGTTTCTGCTACATTGTTAAGAAGGGTGAAGACAGAGTACCTACATTTGAGGAGGTTGAGCTACGGGG
GTGGGGTGGGGATTAGATAAACTGCTGCTTTACTGAAGGCTTTACTATTGCTTATGATAATGTTCATAG
TTGGATATCATATAAAACAGCAAAACCAATTAGGGCAGCTCATCTCCACTCATGATCTAGATCTAGA
TCTCTGTTGGGATCATTGTTTCTGTTGATGCCACTTGTGGTTCTAAGTACTGTGTTTCAAAATGTCAGTTCA
TAGCCTGAAAGAACGAGATCAGCAGGCCCTGTTCCACATACACTCTACATTCTCAGTATGTTTGCACGTTCTAATTCCAT
CAGAAGCTGACTCTAGATCTGAGTCCGGCAGCTAGGCCGTCACCTCAGTGTACAGGTTACCAAGGCTCTCGCTG
TCCGTTGAGCTGACGACACAGGACACGCAAATTAAAGGCCGGCCGTAACCTCTAGTCAGGCTTAAGTGA
TATTACGGACTGCCGCTGTTTACAACGCTGACTGGGAAACCCCTGGCTTACCAACTTAATGCCCTGCAAC
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AATGGCGCTTGTGTAATAAGCCCCCTTCCGGCTTTTTTT

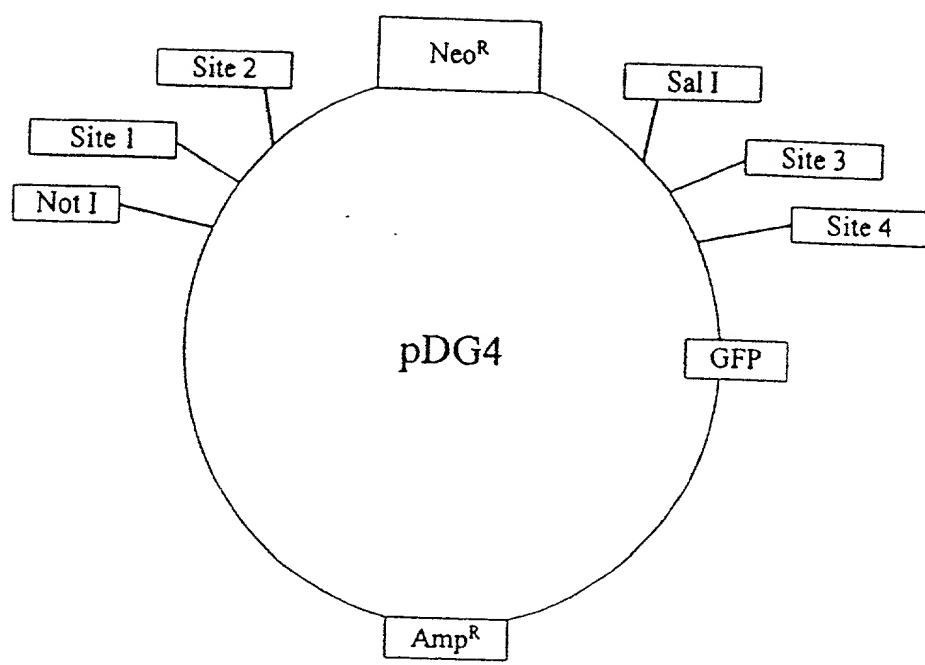


FIGURE 3A

FIGURE 3B

pDG4:

TGCTCCTGCCGAGAAAGTATCCATCATGGCTGATGCAATGCGGCCGCTGCATACGGCTGATCCGGCTACCTGCCATTG
ACCACCAAGCGAAACATCGCATCGAGCGAGCACGTACTCGGATGGAAGCCGGCTTGTGATCAGGATGATCTGGACGAA
GAGCATCAGGGGCTCGCGCAGCGAAGTGTGCGCAGGCTCAAGGCAGCGCATGCCGACGGCGATGATCTGTCGTGAC
CCATGGCGATGCCTGCTTGCAGAATATCATGGTGGAAAATGGCCGTTTCTGGATTCATGACTGGCCGGCTGGGTG
TGGCGGACCGTATCAGGACATAGCGTTGGCTACCCGTGATATTGCTGAAGAGCTTGGCGCGAATGGCTGACCGCTTC
CTCGTGTACGGTATGCCGCTCCGATTGCGAGCGCATGCCCTCATGCCCTCTTGACGAGTTCTTGTGAGGGGA
TCGATCCGCTCTGTAAGTCTGAGAAATTGATGATCTATTAACAATAAAAGATGTCACAAATGGAAGGTTTCTGT
CATACTTGTTAAGAAGGGTGGAGAACAGAGTACCTACATTTGAATGGAAGGATTGGAGCTACGGGGTGGGGTGGGGT
GGGATTAGATAAATGCCGCTTTACTGAAGGCTTTACTATTGCTTATGATAATGTTCATAGTTGGATATCATAA
TTAAACAAGCAAACCAATTAAAGGGCCAGCTCATTCTCCCACTCATGATCTATAGATCTATAGATCTCTCGTGGGAT
CATTGTTTCTCTGATTCCACATTGTTGTTCTAAGTACTGTGTTTCCAATGTGTCAGTTCATAGCCTGAAGAAC
GAGATCAGCAGCCTCTGTTCCACATACACTCATTCTCAGTATTGTTGCAAGGTTCTAATCCATCAGAAGCTGACTC
TAGATCTGGATCCGCCAGCTAGGCCGTGACCTCGAGTGATCAGGTACCAAGGTCTCGCTCTGTGTCGTTGAGCTCG
ACGACACAGGACACGCAAATTAAATTAAAGGCCGGCCGTACCCCTAGTCAGGCTTAAGTGAGTCGTATTACGGACTGG
CCGTGTTTACAACGTCGTGACTGGGAAAACCTGGCTTACCCAACTTAATGCCCTTGCAAGCACATCCCCCTTCGCC
AGCTGGCGTAATAGCGAAGAGGCCGCACCGATGCCCTCCAAACAGTTGCGCAGCCTGAATGGCGAATGGCGCTTCGC
TTGTAATAAGCCGCTCGCGGGCTTTTTTT

FIGURE 3B (Continuted)

Annealing site	Sequence	Sequence after digestion
1	5' tgtgctcctttggcttgcttccaa... 3' 3' acacgaggagaaacccgaaacgggtt... 5'	5' tgtgctcctttggcttgcttccaa... 3' 3' ctggttctgtctggcttgcccaa... 5'
2	5' ctggaaaggaaacccgaaacgggtt... 3' 3' gaccaaggaaacccgaaacgggtt... 5'	5' ctggttctgtctggcttgcccaa... 3' 3' tt... 5'
3	5' ggtccctcgctctgtgtccgttggaa... 3' 3' ccaggaggcggagacacaggaaactt... 5'	5' ggtccctcgctctgtgtccgttggaa... 3' 3' tt... 5'
4	5' ttggcggtccgtgtcgtcgaa... 3' 3' aaacggcacaggacacaggcaggctt... 5'	5' ttggcggtccgtgtcgtcgaa... 3' 3' tt... 5'

FIGURE 4

Annealing site	Sequence		Sequence after digestion	
1	5'	AAtgtgtgtccctttggcttgcgttCCGC	3'	5' AA
	3'	Ttacacgaggagaacccgaacgaaagg	5'	3' Ttacacgaggagaacccgaacgaaagg
2	5'	AAActgggttctgtgtggcttggCCGC	3'	5' AA
	3'	Ttgaccaagaacacgaaaccggg	5'	3' Ttgaccaagaacacgaaaccggg
3	5'	AAAGgtccctcgctctgtgtccgttGAGCT	3'	5' AA
	3'	Ttccaggaggcgagacacaggcaac	5'	3' Ttccaggaggcgagacacaggcaac
4	5'	AAAttgtcggtgttcgtcgAGCT	3'	5' AA
	3'	Ttaaacccacaggacacaggcagc	5'	3' Ttaaacccacaggacacaggcagc

FIGURE 5

FIGURE 6

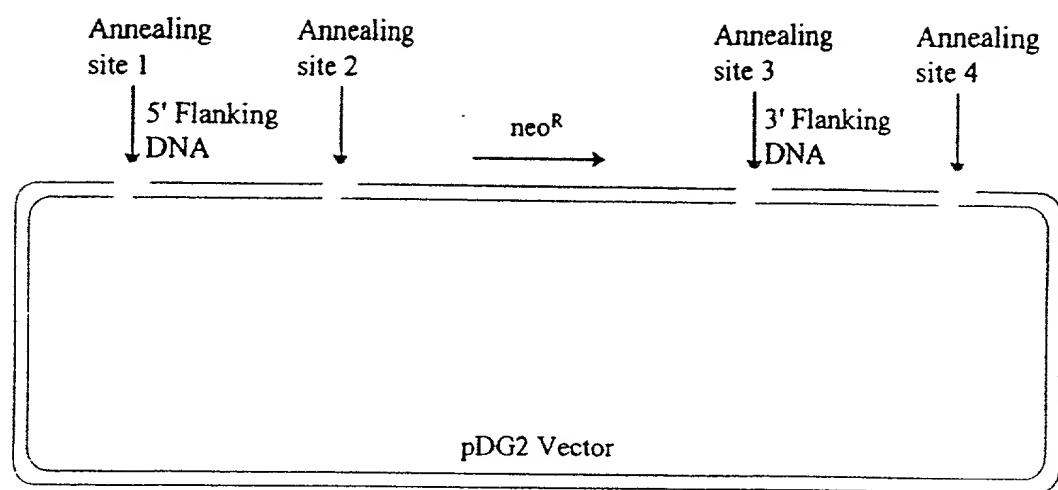
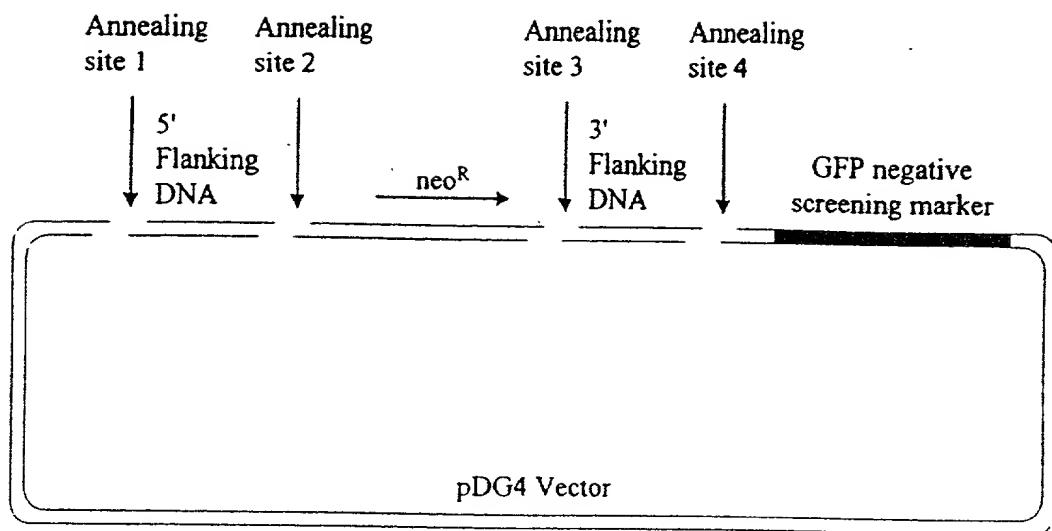


FIGURE 7



TTCCCTGACAAGACTATGTCCACTCAGGAGCCCCAGAAGAGTCTTCTGGGTTCTCTCAACTCCAATGCCAC
CTCTCACCTTGGACTGGCCACCAACCAGTCAGAGCCTGGTGCCTGTATGTGTCATCCCAGATGGCCTC
TTCCCTAGCCTAGGGCTGGTGAAGTCTGGTGGAGAAATGTGCTGGTTGTATAGCCATCACCAAAAACCGCA
ACCTGCACTCGCCCATGTATTACTTCATCTGCTGCCTGGCCCTGTCTGACCTGATGGTAAGTGTCA
CGTGCTGGAGACTACTATCATCCTGCTGGAGGTGGCATCCTGGTGGCCAGAGTGGCTTGGTGCAG
CAGCTGGACAACCTCATTGACGTGCTCATCTGTTCCATGGTGTCCAGTCAGCCTGCTGGCATCA
TTGCTATAGACCGCTACATCTCCATCTCTATGCGCTGCCTATCACAGCATCGTACGCTGCCAGAGC
ACGACGGGCTGCGTGGCATCTGGATGGTCAGCATCGTCTCCAGCACCCCTTTATCACCTACTACAAG
CACACAGCGTTCTGCTGCCTCGTCACTTCTTCTAGCCATGCTGGCACTCATGGCGATTCTGTATG
CCCACATGTTCACCGAGAGCGTGCACAGTCCAGGGATTGCCAGCTCCACAAAAGGCCGGTCCAT
CCGCCAAGGCTTCTGCCTCAAGGGTGTGCCACCCCTACTATCCTCTGGGATTTCTTCTGTGCTGG
GGCCCCCTTCTTCCTGCATCTTGCATCGTCCCTGCCCCAGCACCCCCACCTGCAGCTGCATCTTC
AGAACTTCAACCTTCTCCTCCTCATCGTCCACTGTTGACCCCTCATCTATGCTTTCG
CAGCCAGGAGCTCCGATGACACTCAAGGAGGTGCTGTGCTCCCTGGTATCAGAGGGCGCTGGCAG
AGGGTGACAGTGTATCCAGTGGCCTGCATCTGTGAGACCACAGGTACTCATCCCTTCTGATCTCCATT
TGTCTAAGGGTCGACAGGATGAGCTTAAAGAAACCCAGAGTGCCTGGGCCAGGAGAAAGGGTAAC
TGTGACTGCAGGGCTACCCAGGGCAGCTACGGGAAGTGGAGGAGACAGGGATGGAACTCTAGCCCTGA
GCAAGGGTCAGACCACAGGCTCCTGAAGAGCTTCACCTCTCCCCACCTACAGGCAACTCCTGCTCAAGCC
(SEQ ID NO: 19)

Targeting Vector (5' arm; 200 bp flanking neo insert):

CCGACAACAAACATGAAGTGAATCAGAAGCTGGGGGCTGATACCACCTGGAGCTGCAG
CCTCCACAGACCGCTTCTACTTCCTGACAAGACTATGTCCACTCAGGAGCCCCAGAA
GAGTCTTCTGGGTTCTCTCAACTCCAATGCCACCTCTCACCTGGACTGCCACCAACC
AGTCAGAGCCTGGTGTCTGTATGTG (SEQ ID NO: 20)

Targeting Vector (3' arm; 200 bp flanking neo insert):

GACTACTATCATCCTGCTGCTGGAGGTGGCATCCTGGTGGCCAGAGTGGCTTGGT
CAGCAGCTGGACAACCTCATTGACGTGCTCATCTGTGGCTCATGGTGTCCAGTCT
GCTTCTGGGCATATTGCTATAGACCGCTACATCTCCATCTTCTATGCGCTCGTTAT
CACAGCATCGTACGCTGCCAGAG (SEQ ID NO: 21)

FIG. 8